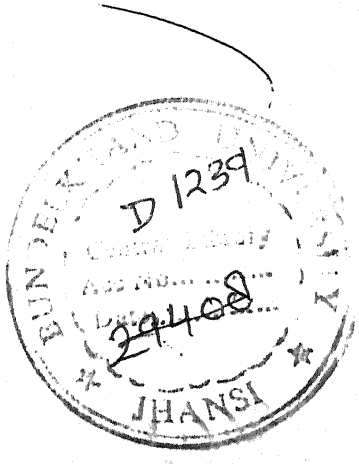
A COMPARATIVE STUDY OF THE EFFECT OF ANTACIDS, CIMETIDINE AND ANTICHOLINERGICS ON GASTRIC pH

Thesis

FOR DOCTOR OF MEDICINE

(ANAESTHESIOLOGY)



BUNDELKHAND UNIVERSITY

JHANSI

1985

PRADEEP KUMAR LAKHANI

C E R T I F I C A T E

This is to certify that the work of Dr. PRADEEP KUMAR LAKHANI on "A COMPARATIVE STUDY OF THE EFFECT OF ANTACIDS, CIMETIDINE AND ANTICHOLINERGICS ON GASTRIC pH" which is being presented by him for M.D.(Anaesthesiology) examination, 1985, has been carried out in the Department of Anaesthesiology.

He has put in the necessary stay in the department as per University regulations.

Dated : 28/July/85

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C E R T I F I C A T E

This is to certify that the work of Dr. PRADEEP KUMAR LAKHANI on "A COMPARATIVE STUDY OF THE EFFECT OF ANTACIDS, CIMETIDINE AND ANTICHOLINERGICS ON GASTRIC pH", which is being presented by him for M.D.(Anaesthesiology) examination, 1985, has been conducted under my personal guidance.

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This is to certify that the work of Dr. PRADEEP KUMAR LAKHANI on "A COMPARATIVE STUDY OF THE EFFECT OF ANTACIDS, CIMETIDINE AND ANTICHOLINERGICS ON GASTRIC pH", which is being presented by him for M.D. (Anaesthesiology) examination, 1985, has been conducted under my personal guidance.

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A C K N O W L E D G E M E N T S

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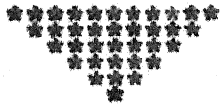
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INTRODUCTION

I N T R O D U C T I O N

'That which can not be easily treated had better be prevented'

J. Alfred Lee, Synopsis of Anaesthesia.

The post-graduate educational number of the British Journal of Anaesthesia, dated March 1963, consists of a symposium entitled "Vomiting and Anaesthesia". In the editorial appear the words, "we do not believe that the pages that follow will be the last words to be written on what is one of the most important causes of pre-operative mortality and post-operative morbidity". In ending the editorial the hope is expressed that the ordinary anaesthesiologist with the help of the scientist would, by advancing the art and dispelling the danger, save the patient from "the black cloud of his own vomiture". The first statement is undoubtedly true.

Whenever the protection afforded the tracheo bronchial tree by the laryngeal reflexes is breached, the patient's life is placed in jeopardy. While this reflex protection is rapidly rendered ineffective by unconsciousnes

or muscle paralysis, even at other times, it by no means, affords total protection.

Vomiting and regurgitation of gastric contents, followed by pulmonary aspiration, is an infrequent but well recognized hazard in the practice of anaesthesia. It is a major cause of post-anaesthetic morbidity and mortality. Silent regurgitation of gastric contents occurs, more frequently than is realized, even with an endotracheal tube in place. The silent regurgitation is more sinister in that there are no active signs initially to warn the clinician of the impending danger.

It would be wrong to think that aspiration occurs only in anaesthetized patient. Pulmonary aspiration may occur while the patient is conscious, as may happen in aspiration of meconium by the newborn, peanuts by the infant, water by the person who nearly drowns and gastric contents by parturient or the patient in an intensive care unit.

The reports on maternal mortality, published in 1969 and 1972, highlighted the increase in the number of deaths attributable to anaesthetic causes which contrasted with the decline in mortality from this cause over the previous decade and to the continued overall decline in maternal mortality. In the 1969 report, nearly 50% of the deaths attributable to the anaesthetic complications

were due to the causes which in the report was termed "avoidable". Of 24 case reports in this document in which death was regarded as "avoidable", inhalation of gastric contents was described as the cause of death in 18 cases (75 percent). The syndrome that develops following inhalation of gastric contents during anaesthesia for obstetric procedures was first reported by Hall (1940) and subsequently by Mendelson (1946). The latter drew attention to the asthma-like syndrome which is the result of inhalation of acid gastric contents producing a chemical pneumonitis. The severity of the lesion depends on the pH of gastric contents. Bannister and Sattilaro (1962) suggested that Critical pH below which symptoms became severe is 2.5. Crawford (1970), however, has recently suggested the pH 3 should be regarded as the critical level. Gastric fluid volumes of 0.4 ml/kg body weight have been stated to incur greater risk. However, Stoelting considers 20 ml (0.3 ml/kg) potentially hazardous. The nature and extent of the damage depend not only on the pH and volume aspirated but also the composition of the aspirate, especially its tonicity and the presence of large particles or food material.

As is commonly believed, this complication of post-anaesthetic aspiration pneumonitis, is not only limited to obstetric anaesthesia alone, but, as evidenced

by the work of Culver, Makel and Beecher (1951) unselected non-obstetrical surgical patients also showed regurgitation in 26.3 percent, aspiration in 16.3 percent and vomiting in 8 percent cases after administration of general anaesthesia. Other studies have confirmed this potential danger in emergency as well as elective operations.

Dinnick (1964), analysing 400 deaths in which anaesthesia was casually related, found 31 non-obstetric patients and 12 obstetric patients in whom regurgitation or vomiting of fluid material was the principal factor. In a recent paper from Auckland, the rate of mortality from pulmonary aspiration syndrome all over hospital, between 1967 and 1969 was 1 in 11000 of non-obstetric patients.

(Hutchinson and Newson, 1975).

The diagnosis of aspiration pneumonitis may be initially confused with pulmonary oedema - the distinction must be made, because the treatment of the two conditions is different. The aspiration of solid material leading to symptoms and signs of bronchial obstruction must be recognised and relieved.

Prevention of the initial insult is the best approach. This can be achieved by meticulous attention to detail and surveillance of gastric emptying by physical

or pharmacological means. The single most important factor in the patho-physiological progression of the syndrome is the degree of acidity of the aspirated material and any means to increase the pH of the gastric contents of patients at risk should be used.

Keeping this problem in mind, the present study was undertaken at M.L.B. Medical College Hospital, Jhansi, with the following aims -

1. To assess the efficacy of oral antacids, Cimetidine and anticholinergic drugs in increasing gastric pH to prevent aspiration pneumonitis.

2. To assess the efficacy of individual drug in producing the desired effect with minimal or no undesirable side effects.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Occurrence of regurgitation and vomiting, with subsequent inhalation of gastric contents into the bronchial tree, is not uncommon and remains an important factor in the morbidity and mortality of anaesthesia. Hall (1940) reported the death of a normal, healthy primigravida which occurred as a result of aspiration of vomit during anaesthesia for a forceps delivery.

Mendelson (1946) described a previously unrecognized pulmonary complication of a general anaesthesia.

The actual aspiration often escaped recognition, but was followed by an "asthmatic like" syndrome with distinct clinical, radiological and pathological features.

There was cyanosis, tachycardia, dyspnoea and bronchospasm, but no mediastinal shift or massive atelectasis. Wheezes, rales and rhonchi were heard sometimes over the affected portions of the lungs. X-ray revealed irregular, soft, mottled densities.

Progressive cardiac embarrassment and pulmonary oedema sometimes supervened.

Mendelson was able to reproduce this syndrome in rabbits using N/10 Hydrochloric acid and un-neutralized human fluid gastric contents. At autopsy, there was congestion and oedema throughout the lungs, a wavy bronchiolar pattern indicative of spasm, with peribronchiolar haemorrhage and exudate, usually with areas of secondary emphysema. The bronchial mucous membrane had sloughed in places.

When normal saline, distilled water or neutralized fluid gastric contents were injected into the rabbit's lung, a brief phase of obstructive respiration ensued, but breathing quickly returned to normal. The lungs showed only minute scattered areas of atelectasis. It was concluded that the features of Mendelson's syndrome could be attributed to the aspiration of gastric Hydrochloric acid.

Later, Teabeaut (1952) found that the pH of acid introduced into the lungs had to be below 2.5 to produce pneumonitis-like tissue reaction, and the gastric secretions of higher pH produced approximately the same tissue response as isotonic saline solution. Also the volume of gastric contents is of importance (Bannister and Sattilaro, 1962; Awe et al, 1966;

Greenfield et al, 1969) and it has been suggested that acid aspiration pneumonitis is most likely to occur when the pH of the aspirated fluid is below 2.5 and the volume exceeds about 20 ml (Vandam 1965; Roberts and Shirley 1974; Stoelting 1978). Taylor (1975) has reported its occurrence with gastric contents at pH 3.5.

PATHOLOGY OF ACID ASPIRATION

Most of the knowledge of the pathologic changes of acid aspiration is based on experiments done on animals. After aspiration, acid is rapidly distributed throughout the lungs, and damage occurs immediately. Acid gastric juice stained with methylene blue and aspirated into an isolated dog lung can be seen on the surface of the lung within 12 to 18 seconds. Isolated areas of atelectasis become visible when the dye appears and become extensive within 3 minutes (Hamelberg et al, 1964). Pathologic examination within the first few hours of acid aspiration reveals epithelial degeneration of the bronchi, pulmonary oedema, and haemorrhage with electron microscopy, necrosis of type I alveolar cells and the presence of free lamellated inclusion bodies in the pulmonary transudate are noted. Within 4 hr, there is an acute infiltration of polymorphonuclear cells, and fibrin can be seen in the alveolar space. Degeneration of alveolar type II cells and further necrosis of type I cells with detachment from the basement membrane can also

be noted. During the next 24 to 36 hr, marked polymorphonuclear infiltration results in alveolar consolidation, and damage to the airways may result in mucosal sloughing. After 48 hr, hyaline membranes can be seen (Greenfield et al, 1969). Gross examination shows lungs that are boggy, oedematous, and haemorrhagic. At 72 hr, resolution has already begun, there is regeneration of bronchial epithelium, proliferation of fibroblasts, and a decrease in acute inflammation (Downs et al, 1974).

Lungs obtained from experimental animals 2 to 3 weeks after acid aspiration usually are normal or slightly increased in weight and show parenchymal scarring with pleural retraction.

PHYSIOLOGY OF ACID ASPIRATION

The severe chemical burn induced by acid aspiration causes loss of alveolar capillary integrity and exudation of fluid and protein into the alveoli and bronchi (Greenfield et al, 1969). Serum protein electrophoresis done on material aspirated from a small bronchus after acid aspiration reveals a pattern identical to that of serum (Awe et al, 1966). This exudation causes increased lung weight, decreased pulmonary compliance, and pulmonary oedema (Greenfield et al, 1969; Cameron et al, 1972; Davidson et al, 1974). The accompanying loss of

intravascular volume may cause severe hypotension (Lewis et al, 1971; Greenfield et al, 1969; Cameron et al, 1972).

Hypoxia can occur within minutes of acid aspiration (Awe et al, 1966; Lewis et al, 1971; Greenfield et al, 1969; Hamelberg et al, 1964; Cameron et al, 1972). It has multiple causes. First, reflex airway closure occurs in response to the aspiration of fluid (Davidson et al, 1974; Halmgyi et al, 1962; Colebatch et al, 1962). Second, surfactant activity decreases when surfactant is destroyed, diluted or altered by acid, this reduction leads to alveolar instability and atelectasis (Awe et al, 1966; Colebatch et al, 1962; Modell et al, 1967). Third, the outpouring of fluid and protein into damaged tissues causes interstitial and alveolar oedema resulting in further airway closure. Finally, alveolar haemorrhage and consolidation occur, followed by hyaline membrane formation. All these conditions contribute to the large alveolar-arterial oxygen differences and significant increase in venous admixture.

Acid aspiration also causes changes in the pulmonary vasculature. Initially, pulmonary artery pressure may rise rapidly (Awe et al, 1966; Hamelberg et al, 1964), however it falls quickly in association

with decreased cardiac output resulting from loss of intravascular volume (Awe et al, 1966; Greenfield et al, 1969). As a consequence, pulmonary artery pressure is usually low or normal (Cameron et al, 1972; Chapman et al, 1974). On the other hand, pulmonary vascular resistance is elevated (Greenfield et al, 1969; Toussaint et al, 1974; Fisk et al, 1970). This may be due to hypoxic vasoconstriction or anatomic obstruction. Marked constriction of pulmonary arterioles has been seen arteriographically (Booth et al, 1972) and histologically (Hamelberg et al, 1964) after aspiration, and in-situ thrombus formation also has been reported (Booth et al, 1972; Cameron et al, 1968).

CLINICAL CORRELATION (Wynne et al, 1977).

The clinical picture produced by aspiration of gastric contents depends on the nature of the material aspirated. Aspirations in humans are termed "acid" if the pH is less than 2.5 and "non-acid" or "neutral" if the pH is greater than 2.5.

Vomiting may produce the aspiration picture of solid particulate matter occluding various parts of the tracheobronchial tree, the physical signs are those of collapse localized to the area distal to the blockade. Death may occur quickly from tracheal or bronchial obstruction, but the sequence of events will depend on the particulate size and position of the occlusion.

The main physiologic distinction between the aspiration of acid and neutral clear liquid is that the acute respiratory decompensation caused by the latter is frequently short-lived and more easily reversible.

If the acidity is less than pH 2.0 and volume is of the order of 0.4 ml/kg, then the full blown picture of aspiration pneumonitis will be seen (Roberts et al, 1974). Lewis, Burgess and Hampson (1971) studied 18 patients with documented aspiration. Although the volume of aspirate was not known, there was a direct relation between mortality and gastric acidity. Particularly alarming was the 100% mortality rate among patients with a gastric pH of less than 1.8. This rate prevailed, despite vigorous supportive measures such as intubation, positive-pressure ventilation and administration of steroids, antibiotics and intravenous fluids. When the gastric pH was between 1.8 and 2.5, however, the mortality rate was only 25%.

Carefully analysed, much of the experimental and clinical information available suggests that the term "Mendelson's syndrome", used to describe severe acid aspiration, may be a misnomer. Mendelson's original work described clinical observations of 66 patients. The character of the aspirated material was known in 45. Five aspirates contained large particles. These patients

presented with symptoms of large airway obstruction. The remaining 40 aspirates were liquid. After aspiration these patients developed an asthma-like syndrome. On the basis of his experimental data, Mendelson assumed this clinical response was caused by acid aspiration. However, the mortality rate in his patients was zero, in marked contrast to experimental studies of acid aspiration and other clinical studies in which mortality rates were as high as 35% to 60%.(Lewis et al, 1971; Cameron et al, 1973; Tinstman et al, 1973; Arms et al, 1974). Furthermore, in about 75% of his patients the course was uncomplicated. Finally, although none of his patients received ventilatory supports, all recovered in 36 hr. The clinical syndrome described in Mendelson's patients resembled only slightly the findings of severe life-threatening pulmonary injury that Mendelson demonstrated experimentally and that we now associate with acid aspiration. Most of the Mendelson's patients may have aspirated only small amount of acid or may have experienced some form of "non-acid" aspiration.

<u>The concept of pH</u> :- The term pH was introduced in 1909 by Sorensen, who defined pH as the negative logarithm of the hydrogen ion concentration.

$$pH = - \log (H^+)$$

This definition, while not rigorous, is adequate for most biochemical purposes. To calculate the pH of a solution :

(1) Calculate hydrogen ion concentration (H^+)

(2) Calculate the base 10 logarithm of (H^+)

(3) pH is the negative of the value found in step 2.

For example, for pure water at 25°C :

$pH = - \log (H^+) = - \log 10^{-7} = - (-7) = 7.0.$

Low pH (acidic) values (below 7.0) correspond to high concentrations of H^+, and high pH (basic) values (above 7.0) to low concentrations of H^+.

Acids are proton donors and bases are proton acceptors. A distinction is made, however, between strong acids (e.g. HCl, H_2SO_4), which completely dissociate even in strongly acidic solutions (low pH), and weak acids, which dissociate only partially in acidic solution. A similar distinction is made between strong bases (e.g. KOH, NaOH) and weak bases (e.g. $Ca(OH)_2$). Only strong bases are dissociated at high pH.

SECRETION OF HYDROCHLORIC ACID BY THE STOMACH (Bannister et al, 1962).

The acidity of the stomach content is one of the primary cause of aspiration pneumonia. Hydrochloric acid

is secreted in a virtually pure state by the oxyntic cells of the gastric mucosa, the undiluted secretions having a titrimetric acidity of 0.17 N and pH of 0.87.

Gastric acid production is primarily controlled by the vagus nerves. Alcohol stimulates the production of large amounts of acid. Personality and emotion play an important part in the gastric secretion. Relaxed or sedated individuals secrete small amounts of acid. Anxiety states, however, result in high rates of acid secretion.

Shay and Sun (1956) reported finding gastric contents of pH 2 to pH 1.3 during fasting and Holmes (1956) found that some women in labour had gastric contents of pH 2.0 to 1.0.

Gastric emptying :- Meal is evacuated from the stomach within two to four hours and normally this is true.

Gastric emptying can be delayed by drugs commonly used for pre-anaesthetic medication and for pain relief. Atropine in doses of 0.4 mg probably does not alter gastric emptying, and antagonizes the effect of morphine. Larger doses of Atropine (0.8 mg) markedly decrease the tonus and motility of the stomach (Goodman et al, 1955).

The stomach is known to empty poorly during high intestinal obstruction. Displacement of the stomach by large tumours may retard evacuation of stomach contents. This situation is encountered in pregnant women at term when the uterus presses the pyloric portion of the stomach upward and backward.

Anxiety and pain have been universally believed to retard gastric emptying.

Applied anatomy of vomiting (Brown, 1963) :- The expulsion through the mouth of material from the alimentary tract is by muscular action. The act of vomiting is preceded by salivation, rapid breathing, pallor, sweating and tachycardia.

Like any other reflex arc, vomiting has its afferent and efferent pathways and its central connexions.

Afferent pathways :- Impulses travel from many parts of the body and ascend in the visceral afferent fibres accompanying the vagus and less importantly, the sympathetic.

Chemical changes occuring in the body do not stimulate the vomiting centre directly but reflexly by stimulating the chemoreceptor trigger zone of Borison and Wang (Borison and Wang, 1953).

The vomiting centre :- This is closely related to other vital centres, e.g. the respiratory and vasomotor centres and the vestibular and salivary nuclei, in the dorsolateral border of lateral reticular formation. The chemoreceptor trigger-zone lies superficial to the true vomiting centre.

Efferent pathways and mechanics of vomiting :- The efferent pathways of vomiting reflex are many and various, both somatic and visceral pathways being involved.

The mechanics of vomiting may be stated as follows (Davenport, 1961). This commences with a deep inspiration followed by closure of the glottis and nasopharynx and is immediately followed by expiration together with contraction of the muscles of the abdominal wall and descent of diaphragm. Now while the body of stomach relaxes, the antrum and also the pylorus and duodenum contract. This propels stomach contents into the oesophagus and mouth, and prevents escape from the stomach via the pylorus. A pressure of 40 cm.H_2O is needed to lift the contents of the stomach into the mouth in the upright position. The cardia is elevated during vomiting so that the abdominal part of the oesophagus rises into the chest (Johnson et al, 1966). While the glottis goes into spasm during the expulsive phase, it soon relaxes, so that aspiration of stomach contents into the bronchial tree is almost bound to

happen in the unconscious supine patient. Pre-disposing factors during anaesthesia include : (a) Hypoxia, (b) Central stimulation during second stage general anaesthesia - either during induction or recovery, (c) Irritation of the base of the tongue or pharynx by airways etc., (d) Breath-holding and cough.

Regurgitation :- Being a passive act, may be silent and unheralded, and so even more potentially dangerous than vomiting. Pre-disposing factors include : (a) The head-down position if the cardia is inefficient. (b) A stomach full of fluid, (c) An indwelling stomach or oesophageal tube.

The cardiac sphincter :- This is both a sphincter and a valve. It remains closed because of :

(1) The presence of an anatomical muscular sphincter (Code et al, 1958).

(2) Folds of thickened mucosa in the oesophagus (Botha, 1958).

(3) The angle at which the oesophagus meets the fundus of the stomach (Marchand, 1955).

(4) The pinch-cock action of the crus of the diaphragm (in two thirds of patients the right crus only).

Integrity of the sphincter :- Its activity is controlled reflexly (Vagus and sympathetic nerves). Its integrity

is not affected by posture, anaesthetics, relaxants, autonomic blocking agents, or injecting the oesophageal mucosa with local analgesics (O'Mullane, 1954). Its integrity is affected and it is made incompetent by :

(1) Anatomical abnormality, e.g. hiatus hernia (Dinnick, 1961).

(2) The presence of a stomach tube,

(3) Passage of anaesthetic gas from above during attempts at I.P.P.V.,

(4) Attempts at active respiration in the presence of respiratory obstruction.

Ingesting antacids, e.g., Magnesium trisilicate, 15 ml. of the B.P.C. mixture 2-hourly, may increase gastrin production and so may tighten up the sphincter. Intravenous Metoclopramide doubles the basic tone of the sphincter (Heitman et al, 1970).

Thus, in normal patients under anaesthesia if the active vomiting reflex is suppressed, no material can regurgitate from the stomach into the oesophagus, no matter what position the patient is in, so long as the valve/sphincter mechanism is not interfered with.

<u>The cricopharyngeal sphincter</u> :- This is at the upper end of the oesophagus at the level of C_6 and is composed of striated muscle. Its action is both voluntary and reflex.

Its integrity is affected by both anaesthetics and relaxants. It acts as a sphincter normally but as a valve when paralysed. Normally it allows fluid to pass from the pharynx into the oesophagus, but not in the reverse direction. When paralysed by relaxants, it tends to obstruct the passage of fluids from the pharynx to the oesophagus, but not in the reverse direction.

The lower part of the oesophagus contains plain muscle which is not affected by relaxants, but the upper part, the cricopharyngeal sphincter, behaves like striped muscle (Sinclair, 1959).

The Hydrodynamics of Regurgitation :- The normal intragastric pressure is 5-7 cm.H_2O and double this in advanced pregnancy. This is well below the pressure required for reflux through the cardia (Spence et al, 1967). Even when the stomach is distended the pressure is unlikely to be greater than 18 cm.H_2O unless there is contraction of the abdominal muscles (O'Mullane, 1954).

If the glottis is maintained at a height in centimetres above the cardia greater than the intragastric pressure in cm.H_2O, i.e. with a head-up tilt of 40-45°, and if the abdominal muscles are prevented from contracting, then regurgitation is unlikely (Snow et al, 1959).

Measurements of intragastric pressure during the fasciculation following injection of Suxamethonium are usually not greatly increased (Dinnick, 1967), but in about 12 per cent of patients a rise greater than 19 cm.H_2O occurs (Elliott, 1968). This evidence might suggest that Suxamethonium should not be used for intubation in such patients even with a high head-up tilt, as gastric contents could be forced up to the glottis by the increase in intragastric pressure. The question needs clarification as reported pressure measurements are not in agreement (Spence et al, 1967; Roe, 1962).

CAUSES OF VOMITING

(a) Vomitable material in the stomach or oesophagus :

(1) Inadequate pre-operative preparation of the patient. Gastric emptying time varies between 4 and 8 hours: it is usually between 5 and 6 hours (Horton, 1965).

(2) In pyloric obstruction.

(3) When there is peritoneal irritation (e.g., perforated peptic ulcer, acute inflammatory lesions etc.).

(4) Blood in the stomach following bleeding from ulcer, tonsil beds, oesophageal varices, or during gastric operations.

(5) Gross abdominal distension,

(6) Glucose solution mistakenly given to diabetic patients by mouth, instead of intravenously,

(7) In case of oesophageal disease, such as pouch or obstruction.

(b) Vomitable material returned into stomach from bowel, as in cases of intestinal obstruction.

(c) When stomach emptying time is delayed :

(1) In woman in labour,

(2) In cases of head injury,

(3) When there is emotional strain associated with pain, accident, and the incident of hospitalisation,

(4) In seriously ill patients,

(5) After drugs, e.g., Opiates.

FACTORS PRE-DISPOSING TO PASSIVE REGURGITATION :

(Dinnick, 1967).

(a) Considerable volume of fluid in stomach :

(1) In the emergency case,

(2) The patient prepared for elective surgery has a variable amount of resting gastric juice. In the nervous patient this is increased in both quantity and acidity.

(b) Incompetence of the cardia :

(1) Hiatus hernia,

(2) Increased vagal tone,

(3) Presence of gastric tube (Nagler, 1963).

(c) Raised intra-abdominal pressure :

(1) Posture, e.g. lithotomy position,

(2) Suxamethonium fasciculations,

(3) Pregnancy, especially where there is a high head or hydramnios.

(d) Lowered intrathoracic pressure : This can occur with deep spontaneous respiration, and is exaggerated when there is respiratory obstruction as in difficult induction of anaesthesia.

(e) Obesity : There is both a raised intra- abdominal pressure (O'Mullane, 1954) and a greater likelihood of respiratory obstruction during induction of anaesthesia, particularly in unskilled hands.

(f) Pregnancy : Incorporating several factors already mentioned.

(g) Relaxation of cricopharyngeus by deep anaesthesia or muscle relaxants.

TIME OF ASPIRATION :

1. At onset of disease or time of injury.
2. During pre-operative preparation and investigation.
3. During transportation of the patient.
4. During induction of anaesthesia - It is during induction of anaesthesia that the hazard is greatest.
5. During Anaesthesia.
6. At the end of operation - Aspiration of vomitus or regurgitated material occurs at the end of operation with nearly the same frequency as it does during induction : it is equally, if not more dangerous.
7. In the recovery room or Intensive Care Unit.
8. In the remote post-operative period.

PREVENTION OF ASPIRATION PNEUMONITIS : (Robert B. Roberts, 1977).

Different methods have been used in the past to prevent this complication. The first principle of prevention is the possession of a high index of suspicion. Any method, which either reduces gastric content volume to below 25 ml or raises gastric pH to above 2.5 can reduce the number of patients at risk.

Emptying the stomach :- Pre-anaesthetic mechanical or pharmacological emptying of the stomach is theoretically ideal. Regular naso-gastric tubes offer no guarantee of

complete emptying, and leaving a tube in-situ during induction may lead to incompetence of the gastro-oesophageal junction, thus facilitating regurgitation. Large bore tubes may be more effective but their use is unpleasant and time consuming, and they still do not guarantee complete emptying. Indeed the use of such tubes may be positively harmful, in that they lull the anaesthesiologist into a false sense of security.

Apomorphine given slowly, 1 to 3 mg intravenously, has been used to stimulate vomiting prior to anaesthesia (Hershenson et al, 1947). Atropine must be available to stop the retching and nausea after the vomiting. This is also an unpleasant procedure and not without risk, circulatory collapse having been reported (Parr, 1956).

Intubation of the conscious patient :- Intubation of the conscious patient has often been recommended. While awake intubation following good local anaesthesia, adequate sedation, and an unhurried approach may be very valuable in certain type of surgical patients, but not for obstetrical cases. The sedation required is hardly appropriate in obstetrics, and if local anaesthetics are applied to the larynx and vomiting occurs during intubation, aspiration can still occur. There should be enough time to carry out awake intubation. Forcing a tube

into a conscious person's trachea without adequate sedation or local anaesthesia is a barbaric procedure.

Position :- Position of patient during induction is another controversial subject. The head down position has been recommended (Dinnick, 1957) because if any vomiting occurs, this position would allow the gastric contents to flow out of the patient's mouth without contaminating the trachea. The major disadvantage of this position, however, is that it may promote passive regurgitation. Many favour a steep head up tilt in order to discourage regurgitation (Snow et al, 1959). Intra-gastric pressure may increase dramatically after Succinyl choline administration (Anderson, 1962; Roe, 1962), and if regurgitation or vomiting does occur, aspiration is almost inevitable. The steepness of the head-up tilt required to prevent regurgitation may make intubation difficult. A small dose of d-tubocurarine given three or four minutes prior to induction helps to prevent the increase in intra-abdominal pressure following Succinyl choline. The lateral position has also been recommended (Mucklow et al, 1963), but this position is foreign to most anaesthetists during induction and makes intubation difficult, if the airway becomes obstructed, the lateral position will enhance vomiting. Cricoid pressure, as advised by Sellick (Sellick, 1961), can effectively seal the oesophagus.

Induction of General Anaesthesia :- (Stark, 1977).

Crash Induction - The term crash induction is not actually clearly defined. However, it can be taken to mean a method by which the patient is taken from a state of unpremedicated consciousness to one where the airway has been secured by the passage of cuffed endotracheal tube in the shortest possible time. The standard approach to this type of technique follows the sequence outlined below.

1. The stomach is emptied of all fluids by aspiration through a nasogastric tube. The tube is removed before induction of anaesthesia.

2. All monitoring equipment is secured and an intravenous infusion is set up before anaesthesia is induced.

3. The supine jackknife position, head raised (40 - degree, head-up position), is assumed for induction.

4. Pre-oxygenation is performed for 3 to 5 minutes.

5. A competitive blocker is pre-administered.

6. The intravenous induction by a pre-selected dose of Barbiturate or Ketamine is followed by a generous dose of at least 100 mg of Suxamethonium in the 70 kg adult.

7. Cricoid pressure is applied. As soon as the intravenous agent is given, Sellick's maneuver is performed. Sellick (1961) applied backward pressure of the cricoid cartilage against the cervical vertebrae to occlude the oesophagus (a) to control regurgitation of stomach or oesophageal contents during induction of anaesthesia, or (b) to prevent gastric distension from positive pressure ventilation applied by face piece or mouth to mouth respiration.

8. Intubation is carried out as expeditiously as possible.

9. When the trachea is secured, patient is rapidly restored to the supine or slightly head-down position.

10. Anaesthesia is continued as dictated by the clinical circumstances.

11. During and at the termination of anaesthesia, persistent efforts are made to empty the stomach.

12. Extubation is performed in the lateral, head down position after the lungs have been filled with pure oxygen and the patient is clearly able to maintain his own airway.

ACID PROPHYLAXIS

In his original paper Mendelson suggested the use of warm antacids both as an emetic and a buffer for residual acid.

The use of mist Magnesium trisilicate B.P. is well established in obstetric practice, following the report of Taylor and Pryse-Davies (1966).

Peskett (1973) in a further clinical evaluation of the effectiveness of Magnesium trisilicate, showed that the number of patients with a pH of 2.5 or below at emergency caesarean section was reduced from 43.5 to 8.5 percent.

Roberts and Shirley (1974) showed conclusively that the use of antacids prior to caesarean section reduced the number of patients at risk from one in four to one in 48.

Hester and Heath (1977) strongly urged the use of mist Magnesium trisilicate pre-operatively. However, drawbacks are apparent. These include decreased effectiveness with time, associated increase in gastric volume, inconsistency in pH changes, increase in gastric emptying time, and possible pneumonitis from aspirated antacid (Gibbs et al, 1979). Antacids also interfere with absorption or excretion of other drugs. Bioavailability of Cimetidine is reduced from 3 to 48% in subjects taking antacids concurrently (Bodemar et al, 1979).

ANTICHOLINERGICS

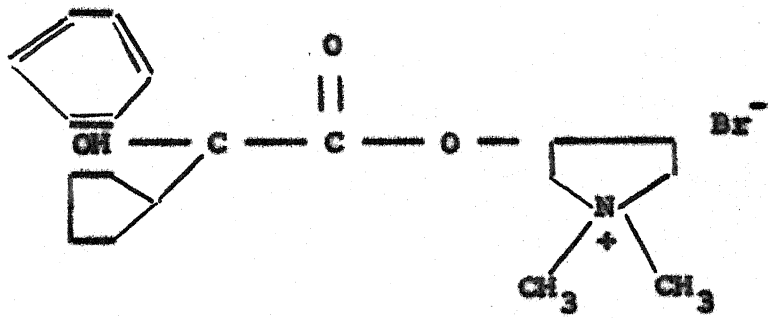
It has been accepted that gastric acid production is primarily controlled by the vagus nerve. Anticholinergic medications inhibit gastric juice production and acidity and increase the resistance of gastro-oesophageal angle to reflux. The degree of inhibition, however, is not the same with all drugs. The anticholinergic quaternary Ammonium compound; Glycopyrrolate, suppresses gastric secretion much more than Atropine or Scopolamine.

Atropine sulphate causes no appreciable reduction in gastric pH, although volume of secretion is apparently reduced.

In comprehensive pharmacologic studies reported by Franko et al (1962), the quaternary Ammonium agent Glycopyrrolate manifested an anticholinergic property, with potency similar to that of Atropine, but more importantly, their studies revealed that Glycopyrrolate possessed a high degree of selectivity for peripheral cholinergic sites relative to that shown by Atropine. It was inferred from their studies that Glycopyrrolate would have lesser CNS effect than Atropine, presumably through the poor penetrating ability across the blood brain barrier afforded by the quaternary Ammonium feature.

Report on the effect of Glycopyrrolate alone on gastric acidity is equivocal. Keating, Black, and

Watson (1978) showed that Glycopyrrolate 0.4 mg i.m. given to non-obstetric patients 60 min before operation had little effect on gastric pH. Similarly, Stoelting (1978) showed that administration of Morphine and Glycopyrrolate 0.2 mg was not significantly different from administration of Morphine alone in decreasing gastric acidity immediately following induction. However, Baraka and others (1977) demonstrated in parturient patients that administration of Glycopyrrolate 0.4 mg i.m. produced a reduction in gastric acidity which was significantly different from that produced by Atropine.



Structure of Glycopyrrolate - 1 Methyl - 3 Pyrrolidyl - Phenyl - Cyclopentane glycolate methobromide.

H-2 RECEPTOR ANTAGONISTS :- (Feely et al, 1983).

With the introduction of Cimetidine an effective gastric H-2 receptor antagonist, pre-anaesthetic prophylaxis against acid aspiration pneumonia may become a reality. Histamine receptors have not so far been

identified by physical or chemical methods but they can be classified pharmacologically by means of antagonists. As a result of inventiveness of James Black and his colleagues (1972), the theoretical concept of a second class of Histamine receptors became a therapeutic reality. The failure of classic anti-histaminic drugs (more appropriately H-1 receptor antagonists) to block the actions of Histamine, particularly on gastric acid secretion but also on isolated heart and uterine muscles, may now be explained by the existence of both H-1 and H-2 receptors which can be blocked by their respective specific H-1 or H-2 antagonists.

Classification of Histamine Receptors

Location	Effect of stimulation	Antagonists
H-1 receptors :		
Blood vessels	Vasodilatation, increased capillary permeability.	Diphenhydramine promethazine etc. Also have anti-cholinergic and sedative effects. Newer agents such as Terfenadine are more specific.
Smooth muscle, bronchi	Contraction	
Skin	Triple reponse, itch.	
H-2 receptors :		
Stomach	Gastric acid secretion	Cimetidine.
Heart, Blood vessels, uterus	Function not established in man.	Ranitidine.

Fortunately, the H-2 antagonists inhibited not only the stimulatory effects of Histamine on gastric acid secretion but also the action of all other gastric stimulants. As a result these drugs have been used to treat disorders in which gastric juice is thought to be aetiologically implicated, and they have proved effective in managing peptic ulceration. These are also being used for all sorts of non-specific alimentary complaints. Although the incidence of adverse reactions to H-2 antagonists in current use is low, such indiscriminate misuse results not only in needless expense but is also potentially dangerous because proper investigation and treatment may be delayed.

To date four such compounds have appeared, Burimamide, Metiamide, Cimetidine and Ranitidine. Neither Burimamide nor Metiamide are, however, likely to be used clinically, the former because it is poorly absorbed from the gastro-intestinal tract and the latter because of occasional bone marrow depression. This adverse effect is thought to be due to the thiourea residue present in the molecule, rather than to H-2 antagonism as such. If so, then Cimetidine, which lacks this particular residue, should prove safe.

CIMETIDINE :- A recently developed Histamine H-2 receptor antagonist, Cimetidine, has been demonstrated

to suppress basal, meal-stimulated and nocturnal gastric secretion. The drug has proved effective in the treatment of peptic ulcer, and no significant side effects have been noted (Burland et al, 1975; Henn et al, 1975; Pounder et al, 1976).

Husemeyer et al (1978) suggested that Cimetidine may be effective as a prophylaxis against acid pulmonary aspiration (Mendelson's syndrome).

Weber et al (1979) suggested that premedication with intra-muscular Cimetidine produces a greater and more consistent rise in gastric pH than does oral Cimetidine.

Coombs et al (1979 a) showed that pre-operative intra-venous Cimetidine is an effective adjunct to good anaesthetic technique which will reduce the risk of pulmonary damage in a patient who aspirate while receiving anaesthesia.

Kirkegaard et al (1980) in a controlled randomized double-blind trial, studied the value of Cimetidine as prophylaxis against acid aspiration pneumonitis. Compared to placebo, Cimetidine reduced the volume as well as the acidity of gastric contents significantly.

After ingestion Cimetidine is rapidly and almost completely absorbed, with a bio-availability approximating to 70% of the available of an i.v. dose. Peak drug concentration occurs 30-90 minutes after ingestion in fasting subjects, but are delayed by about an hour when taken with food. Although a Sulphoxide metabolite is produced in the liver, most of the drug is excreted unchanged by the kidneys so that Cimetidine accumulates in patients with renal insufficiency and in the elderly. Renal tubular secretion of Cimetidine is likely because its renal clearance exceeds G.F.R. Competition with renal secretion of Creatinine may explain the transient rise in serum Creatinine concentration that often occurs during the first few weeks of treatment with Cimetidine.

Cimetidine crosses the placenta into the foetal circulation. Similarly, penetration of the blood brain barrier is presumed to occur, since Cimetidine has been detected in both CSF and brain tissue. The possibility of an interaction with cerebral H-2 receptors may account for the mental confusion, drowsiness and disorientation that sometimes occurs in patients with renal or combined renal and hepatic failure and in the elderly.

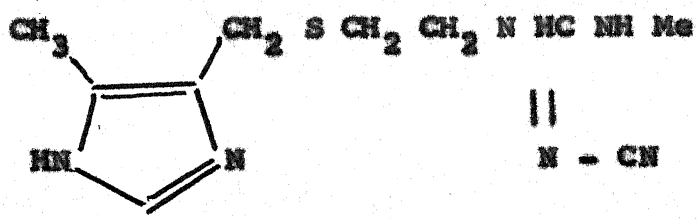
The elimination half life of Cimetidine is about two hours. The duration of action may be prolonged

by increasing the dose of the drug which produces suppression of gastric secretion for upto eight hours.

Cimetidine is given by mouth or by injection. Intra-venous use is restricted to emergencies, such as patients undergoing intensive care or treatment of upper gastro-intestinal haemorrhage. Since hypotension may follow rapid intravenous administration, the drug should be given by slow injection lasting five to ten minutes or, better still, in an i.v. infusion of either saline or dextrose. Cimetidine may also be given intra-muscularly. The usual dose for healing for duodenal and gastric ulcers is 1 gm/day in divided doses of 200 mg after meals and 400 mg before sleep. Recently 400 mg twice daily has also been recommended and in the United States four tablets of 300 mg are used. For prevention of ulcer relapse, 400 mg at night is the most widely used regimen. The duration of maintenance regimen is not yet known, but ulcer relapses have occurred after as long as five years of maintenance treatment with Cimetidine, so that even longer term continuous treatment is necessary to control the periodic activity of ulcer disease.

Two actions of Cimetidine that appear to be unrelated to H-2 antagonism are its effects on the endocrine system and on hepatic drug metabolism. After i.v. injection of Cimetidine, concentrations of

circulating prolactin increases. In vitro, Cimetidine competes for androgen binding sites and although anti-androgenic effects have been reported in man, these are clinically usually unimportant. Gynaecomastia has been seen, particularly with high dose of Cimetidine and is reversible on withdrawal of the drug. It reduces the clearance of many drugs (including Warfarin, Diazepam, Chlordiazepoxide, Phenytoin and Propranolol) that are eliminated by oxidative metabolism. The metabolism of drugs that are primarily conjugated (Benzodiazepines - Lorazepam, Oxazepam) does not seem to be altered. Interference with elimination, and consequent accentuation of pharmacological effects, is of particular importance for drugs such as Warfarin and Phenytoin that have a low therapeutic index. Cimetidine also seems to reduce liver blood flow and thereby decreases the systemic clearance of drugs that are highly extracted by the liver, such as Lignocaine and Propranolol.



Chemical structure of Cimetidine.

CURRENT TREATMENT :- (Chapman, R.L. Jr., 1977) :

Aspiration of particulate matter requires immediate endotracheal suctioning and, if unsuccessful,

bronchoscopy. Particulate matter may become lodged in the large or medium sized bronchi, resulting in lobar atelectasis and mediastinal shift. If the matter is not removed promptly, the atelectatic areas may become infected, causing pneumonia and abscess. However, bronchoscopy is not usually necessary when liquid is aspirated because the fluid can be removed by a combination of postural drainage, percussion, vibration and suctioning.

The larger the volume and the lower the pH, the more severe the reaction. A patient may have respiratory distress immediately after aspiration, or it may occur progressively over a number of hours. Aspiration of material with a pH lower than 2.4 causes destruction of pulmonary surfactant, breakdown of the normal lung structure, and an outpouring of fluid into the lungs. The alveoli and airways become either collapsed or fluid filled, causing abnormal ventilation/perfusion ratios and intra-pulmonary shunting, resulting in hypoxemia. Since plasma is lost into the lungs as pulmonary oedema, the patient may become hypovolemic, manifested most obviously by hypotension and tachycardia. The hypotension accentuates the hypoxemia, and delivery of oxygen to the periphery is less efficient.

If the PaO_2 is greater than 60 torr, if there is no respiratory distress, and if the vital signs are

within normal limits, then therapy consisting of supplementation of oxygen, coughing, and deep breathing exercises usually will suffice. When significant aspiration occurs i.e. sufficient volume with pH less than 2.4, cardio-pulmonary function will be more severely altered, and the patient requires immediate and vigorous therapy.

The upper airway should be cleared of all debris and vomitus, and the trachea intubated with a low-pressure, cuffed, implant-tested endotracheal tube. One hundred per cent oxygen should be administered and the tracheo-bronchial tree suctioned. Lavage with a large volume of any solution has not been shown to be beneficial in removing aspirated gastric contents. In the past, solutions of sodium bicarbonate, corticosteroids, and saline have been recommended for lavage of aspirated material. However, lavage with Sodium bicarbonate is unnecessary because aspirated acid is neutralized quickly by the tracheo-bronchial mucosa; lavage with corticosteroid solution actually increases the number of lesions seen on microscopic and gross inspection of the lungs (Taylor et al, 1968), and lavage with saline solution decreases compliance and increases intra-pulmonary shunt (Awe et al, 1966). Therefore, lavage following aspiration should be limited to removing inspissated secretions, and only small amounts (2 to 4 ml) of saline solution should be used.

MECHANICAL VENTILATION

Arterial oxygenation is improved by decreasing the intra-pulmonary shunt and ventilation-perfusion inequalities with PEEP, which expands collapsed and fluid-filled airways and thereby increases the functional residual capacity. However, in a hypovolemic patient, PEEP can retard venous return, resulting in decreased cardiac output and accentuated hypoxemia. Because plasma is lost into the lungs as pulmonary oedema, vascular volume must be re-expanded with balanced salt solutions, such as Ringer's lactate or appropriate blood products. Adequate fluid replacement is determined by noting blood pressure, pulse, volume of urine output, and central venous pressure (CVP). Because CVP measurements can be inaccurate in severely ill patients, it is preferable to insert a pulmonary artery (PA) catheter so that pulmonary capillary wedge pressure (PCWP) can be measured. In the absence of mitral valve disease, PCWP will approximate left ventricular end-diastolic pressure, giving a better indication of actual vascular volume. In a patient who is hypoxic or acidotic, or both, CVP may be elevated as a result of increased pulmonary vascular resistance, although PCWP will not be elevated in such a patient.

While the plasma volume is being re-expanded PEEP must be adjusted to an optimum level: the level

that results in the best oxygenation of the patient without adversely affecting cardiac output. Oxygenation can be quantitated most accurately by determining venous admixture or intra-pulmonary shunt. The determination requires access to mixed venous blood, which is readily available if a PA catheter has been used. When a PA catheter is used, the arterial-venous oxygen content difference ($Ca-\bar{V}o_2$) can be determined. Changes in cardiac output will vary indirectly with changes in $Ca-\bar{V}o_2$.

In treating acute respiratory failure, including aspiration pneumonitis, intermittent mandatory ventilation (IMV) with PEEP is preferable than controlled mechanical ventilation (CMV) with PEEP. IMV combines a constant rate mechanical ventilator with a continuous oxygen enriched gas flow and allows spontaneous ventilation between mechanical (mandatory) breaths. Since spontaneous respirations are maintained with IMV, intrapleural pressure decreases below its base-line level with inspiration. This allows better venous return, which augments cardiac output. This also occurs when IMV and PEEP are combined, but the patient's vascular volume must frequently be re-expanded before PEEP can be used optimally. It has been documented (Downs et al, 1975; Kirby et al, 1975; Kirby et al, 1975) that in animals and in patients who have adequate vascular volume, circulatory stability is maintained even when high-level PEEP with IMV is used. This stability results because

the mean intra-pleural pressure is less than it is when the same level of PEEP is administered with CMV. With this approach, the IMV rate is set to maintain a level of carbon dioxide tension that permits the patient to have a pH equal to or greater than 7.35 in the absence of metabolic acidosis. The level of PEEP is titrated to produce the lowest venous admixture without decreasing cardiac output.

Discontinuation of Ventilation :- As therapy progresses and the overall condition of the patient improves, extubation can be considered when the following criteria are met :

1. Venous admixture on a fraction of inspired oxygen (F_{IO2}) of 0.3 is less than 15 per cent, or PaO_2 on an F_{IO2} of 0.3 is greater than 60 torr.

2. The level of PEEP is 5 cm.H_2O or less.

3. The IMV rate is 1 per minute or less, and

4. The adequacy of ventilation, as indicated by carbon dioxide tension and pH, does not reveal uncompensated respiratory acidosis.

If IMV is not employed, other standard criteria for discontinuation of controlled ventilation may be used :

1. Alveolar-arterial oxygen tension gradient while breathing 100 per cent oxygen ($A\text{-}aDo_2^{1.0}$) less than 300 torr..

2. Vital capacity greater than 15 ml per kilogram of body weight, and

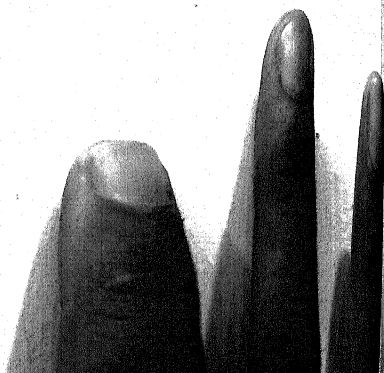
3. Inspiratory force greater than -20 cm.H_2O (Feeley et al, 1975; Pontoppidan et al, 1970).

The patient then breathes 40 per cent oxygen for 15 minutes with a T-piece adaptor while vital signs are monitored closely. If hypercapnia with a pH less than 7.25 or a PaO_2 less than 70 torr does not occur, weaning and extubation usually can be accomplished in 2 to 4 hours.

Other forms of Therapy :- The effectiveness of using parenteral corticosteroids in treating aspiration pneumonitis is debatable, but little experimental evidence exists currently to support the use of parenteral corticosteroids in reversing pathological conditions and improving the clinical course of aspiration pneumonitis. On the other hand, well established evidence exists to support the use of a proper ventilatory pattern to reverse intra-pulmonary pathological conditions caused by aspiration of acidic gastric contents (Chapman et al, 1974; Chapman et al, 1974; Downs et al, 1974).

There is little evidence to show that administering prophylactic, broad-spectrum antibiotics

alters the course of aspiration pneumonitis. Gram stains and cultures of the tracheal aspirate should be taken daily, and antibiotics should be used when clinical evidence and results of cultures indicate that bacterial pneumonia exists.



MATERIAL AND METHODS

MATERIAL AND METHODS

The present study was conducted on 80 adult patients of either sex, of ASA grade I and II, between the ages of 18 and 60 years, at M.L.B. Medical College Hospital, Jhansi, comingin for various routine surgeries, from July 1983 to April 1984.

Every selected patient was carefully inquired about his ailments and history was recorded. The patient was then thoroughly examined physically. Any patient exhibiting any disease or taking a drug, which alter gastric secretion or motility was excluded from this study. All the information was recorded on a pre-designed proforma. All these cases were kept on 6 hours fasting.

Patients excluded from the study :-

1. Patients exhibiting following diseases -
 - Gastric ulcer,
 - Duodenal ulcer,
 - Carcinoma stomach,
 - Reflux oesophagitis,
 - Hiatus Hernia,
 - Diaphragmatic Hernia.

2. Patients taking following drugs -

- Diazepam and/or other sedatives,
- Cimetidine,
- Oral antacids,
- Anti-cholinergics,
- Metoclopramide.

All the selected patients were divided into five groups of 16 patients each depending on the drug/ drugs given. Every patient was given Diazepam 10 mg orally with 30 ml of water to allay his/her anxiety an hour before induction of anaesthesia.

Group A (Antacid group) :- All the patients of group A were given Antacid (Digene gel*®) 30 ml. an hour before induction of anaesthesia.

Group B (Oral Cimetidine group) :- All the patients of group B were given Cimetidine 300 mg. orally an hour prior to induction of anaesthesia.

Group C (Intravenous Cimetidine group) :- All the patients of group C were given Cimetidine 300 mg i.v. (Inj. Tagamet®) an hour prior to induction of anaesthesia.

Group D (Anticholinergic group) :- All the patients of group D were given Atropine sulphate 0.65 mg. i.m. an hour prior to induction of anaesthesia.

*Digene gel - Methylpolysiloxane 25 mg, Mag. hydrox. 185 mg. Alum hydrox. gel to 10 ml, Sod.Carboxy methyl cellulose 100 mg, per 10 ml.

Group E (Oral Cimetidine + Anticholinergic group) :- All the patients of group E were given Cimetidine 300 mg orally + Atropine sulphate 0.65 mg. i.m. an hour before induction of anaesthesia.

Method of collection of samples :- A wide bore naso-gastric tube was passed as smoothly as possible without disturbing the patient, and its presence was confirmed by auscultation over epigastrium, and stomach made empty every time, samples were withdrawn. Gastric samples were taken as follows -

I sample - Just before giving any drug.

II sample - One hour after giving drug just before induction of anaesthesia. pH of both the collected samples were determined by expanded scale pH meter and readings were recorded.

Technique of pH determination :- Gastric fluid pH was determined by Elico expanded scale pH meter model L_I-15. It is a versatile laboratory precision pH meter that permits to read pH directly to an accuracy of $\pm$ 0.02 pH.

Controls and their functions :-

1. On/off switch : This is a rocker type of switch to switch mains to the instrument. In off position, it shorts the meter to protect it when meter is not in use.

2. Meter : This is 100-0-100 microammeter calibrated 0 to 14 pH (+700 mv to -700 mv) on top scale and -1 pH to +1 pH (-100 mv to +100 mv) on bottom scale.

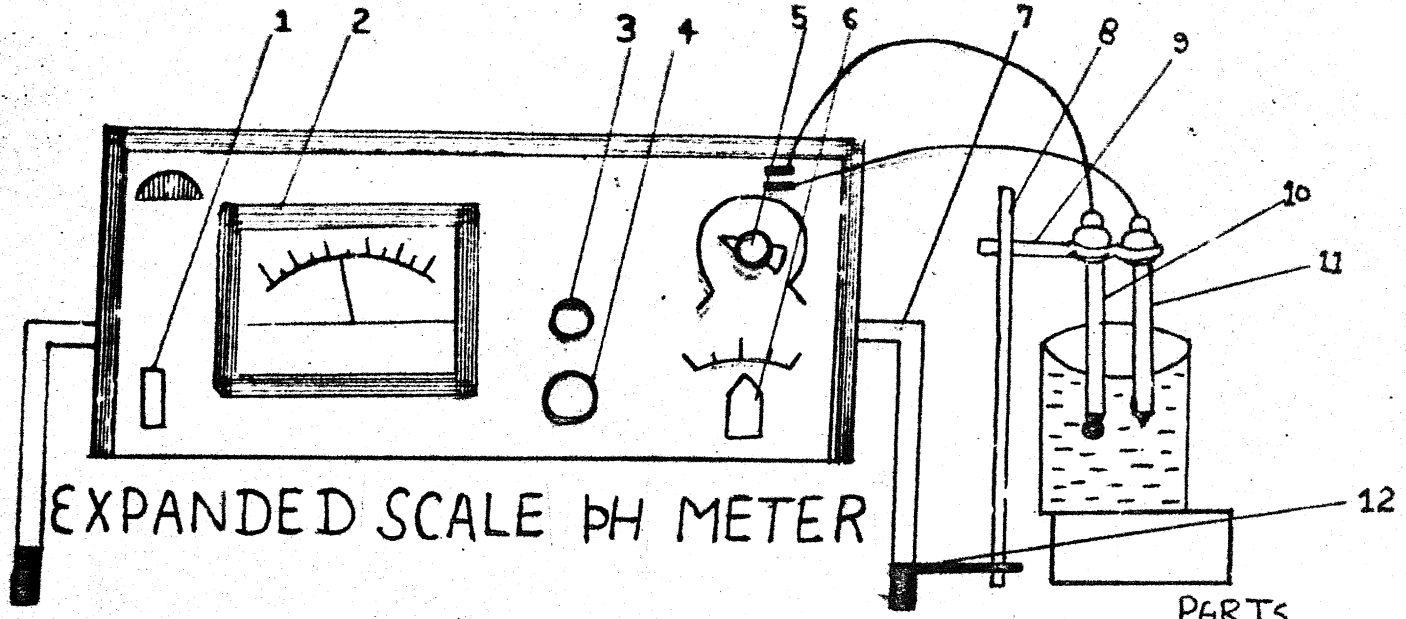
3. Standardise : This is an assymmetry control to make the pH meter read a standard buffer value on meter.

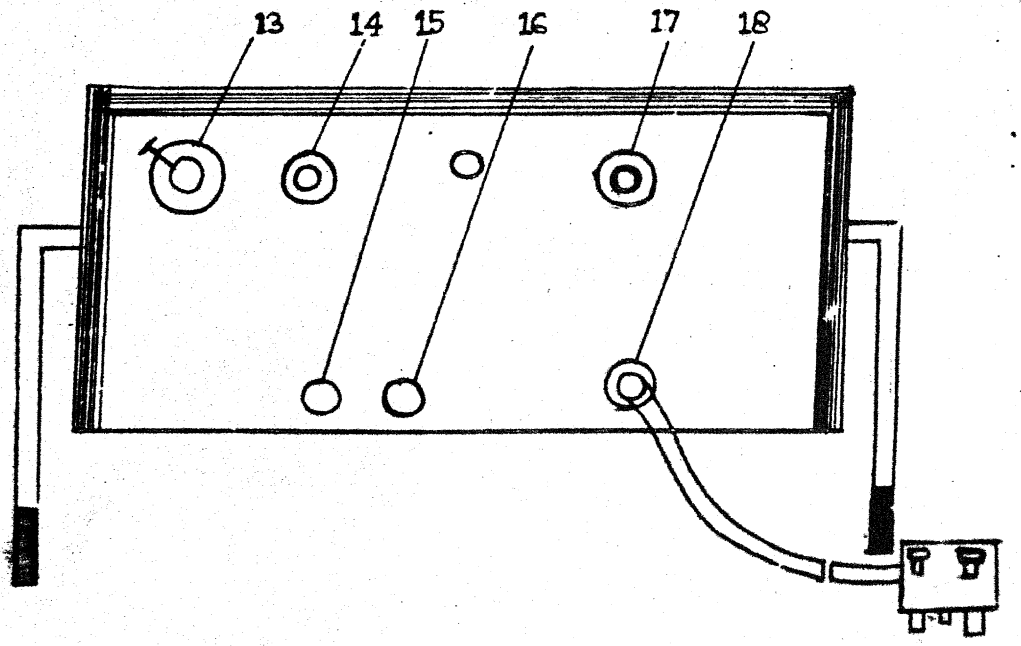
4. Temp. compensate : This is a manual temperature compensation arrangement to correct for the temperature characteristics of the electrodes.

5. Selector : This is a band switch to select any of the Fine functions of instrument. In Std. By position, the amplifier input is shorted and meter should read 7 pH. In normal pH position, it works like an ordinary pH meter to read from 0 to 14 pH with an accuracy of $\pm$ 0.1 pH. In normal mv position, $\pm$ 700 milli volts can be measured. In expanded pH position, pH scale can be expanded by $\pm$ 100 mv.

6. Stand : This is a support to the instrument with a facility to swivell the instrument to set it at a convenient angle for reading.

7. Stand Base and Rod : This is a plated aluminium piece to be screwed to the stand for supporting a rod called electrode stand and supports electrodes with a clip.





PARTS

1. ON/OFF SWITCH
2. METER
3. WINDOW
4. STANDARDISE
5. TEMP. COMPENSATE
6. SELECTOR
7. STAND
8. ELECTRODE STAND
9. CLIP
10. GLASS ELECTRODE
11. RERERENCE ELECTRODE
12. BASE PLATE
13. GIE BUSH
14. RE BUSH
15. PH CAL
16 TMV CAL
17. FUSE
18 POWER CABLE

Fig. No. 1 - Showing Expanded Scale pH Meter,

8. Electrode Rod : Supports the electrodes.

9. Electrode clip : This clip holds both glass and reference electrodes and can be fixed in any convenient height.

10. Reference Electrodes : This is an electrode that serves as reference in ionic flow. The sleeve should always be removed during measurement so that the filling hole is open to atmosphere.

11. Glass Electrode : Main pH sensing electrode.

12. GE socket : This is a socket to accept the glass electrode jack. The screw must be tightened after the jack is inserted into it fully.

13. Fuse : A fuse of 0.5 A to protect the instrument from short circuit.

14. RE socket : This is a banana terminal to which reference electrode pin is connected.

15. Cable : 3 core power cable to connect 230 V 50 Hz mains to the instrument.

16. Mv cal : Preset to calibrate instrument in mv position.

17. pH Cal. : Preset to calibrate instrument in pH position.

OPERATING PROCEDURE

Normal pH measurement :- If pH of any solution is needed to be measured upto the accuracy of ± 0.02 pH, it is essential to use an expansion scale. But the value of pH to the accuracy of first decimal should be found out first. For this Normal pH measurement is to be done. Gastric fluid pH was measured in normal mode of measurement with an accuracy of ± 0.1 pH. Procedure adopted was as follows :

1. Glass and reference electrodes were fixed to the clip and inserted on to the electrode rod which was fitted to the electrode stand base.

2. The electrode stand base was fixed on to the leg of stand of pH meter.

3. Glass and reference electrode jacks were connected to respective sockets.

4. The electrodes were cleaned with distilled water and wiped with filter paper.

5. The electrodes were dipped in 4.00 pH Buffer and temp. comp. adjusted to the temperature of Buffer.

6. The instrument was switched ON and the selector was switched to Normal pH position.

7. Standardise control was adjusted to make the meter read 4.00 pH.

8. It was checked for the repeatability. The selector was switched to Std. By position.

9. The electrodes were removed and cleaned in distilled water and wiped with filter paper.

10. The electrodes were dipped in an unknown solution whose pH was of interest and the temp. comp. was read, if the temperature of solution was different.

11. The selector was switched to Normal pH position to read the value of pH. Steps 8 and 9 were repeated.

OBSERVATIONS

OBSERVATIONS

In the present work the effect of antacids, cimetidine and anticholinergics were observed on gastric pH. To fulfill the purpose of study it was approached in the following way -

A) Total 80 cases were studied which were divided into 5 groups of 16 patients each as shown in table 1.

Diazepam 10 mg orally was given to every patient to allay his/her anxiety. An appropriate size naso-gastric tube is passed and Ist sample of gastric fluid taken and pH recorded.

B) Patients were given different drug/drugs according to their group an hour prior to induction of anaesthesia. Second sample of gastric fluid was taken exactly an hour after the drug administration, just before induction of anaesthesia and pH recorded.

Table 1

Showing distribution of cases into different groups according to the drug/drugs they received.

S.No.	Group	Drug/Drugs	No.of cases	(%)
1.	A	Antacid 30 ml orally	16	(20)
2.	B	Cimetidine 300 mg orally	16	(20)
3.	C	Cimetidine 300 mg i.v.	16	(20)
4.	D	Atropine 0.65 mg i.m.	16	(20)
5.	E	Cimetidine 300 mg orally + Atropine 0.65 mg i.m.	16	(20)
	Total		80	

Total eighty patients were studied. They were divided into five equal groups of sixteen each, depending upon the drug/drugs administered as shown above in table 1.

Table 2

Showing age-distribution in patients.

Age groups (years)	Group A No.	Group B No.	Group C No.	Group D No.	Group E No.	Total No. (%)
11 - 20	2	3	1	2	1	9 (11.25)
21 - 30	6	5	6	5	5	27 (33.75)
31 - 40	5	4	3	6	3	21 (26.25)
41 - 50	1	4	5	2	4	16 (20.00)
51 - 60	2	-	1	1	3	7 (8.75)
Total	16	16	16	16	16	80

Maximum number of cases (33.75%) belonged to age-group 21-30, as shown above in table 2. Average age of the patients studied was 35.475 year. Youngest and oldest of the patients studied were 18 and 60 years old respectively.

Table 3

Showing sex distribution in patients.

S.No.	Group	M		F		Total
		No.	(%)	No.	(%)	
1.	A	8	(50.00)	8	(50.00)	16
2.	B	7	(43.75)	9	(56.25)	16
3.	C	8	(50.00)	8	(50.00)	16
4.	D	10	(62.50)	6	(37.50)	16
5.	E	9	(56.25)	7	(43.75)	16
Total		42	(52.50)	38	(47.50)	80

Males and females were nearly distributed equally in all the groups as shown above in table 3.

Table 4

Showing mean weight in different groups.

S.No.	Group	Mean weight (kg.)
1.	A	47.88
2.	B	48.44
3.	C	49.31
4.	D	48.75
5.	E	50.38
Mean weight		48.952

Mean weight of 80 patients was 48.952 kg. It was roughly same in all the groups as shown above in table 4.

Table 5

Showing distribution of patients according to ASA grading.

S.No.	Group	ASA grade I		ASA grade II		Total
		No.	(%)	No.	(%)	
1.	A	6	(37.50)	10	(62.50)	16
2.	B	7	(43.75)	9	(56.25)	16
3.	C	11	(68.75)	5	(31.25)	16
4.	D	8	(50.00)	8	(50.00)	16
5.	E	6	(37.50)	10	(62.50)	16
Total		38	(47.50)	42	(52.50)	80

All the patients belongedto ASA grade I and II. In ASA grade I, there were 47.50%, and in ASA grade II, there were 52.50% cases as shown above in table 5.

Table 6

Showing type of surgery done.

S.No.	Type of surgery	No.	%
1.	General surgery	35	43.75
2.	Orthopaedic surgery	13	16.25
3.	Obstetric and Gynaecological surgery	18	22.50
4.	ENT surgery	11	13.75
5.	Ophthalmic surgery	2	2.50
6.	Dental surgery	1	1.25
	Total	80	

Patients undergoing different surgical operations were studied. Maximum number of patients were of General surgery (43.75%) as shown above in table 6.

Table 7

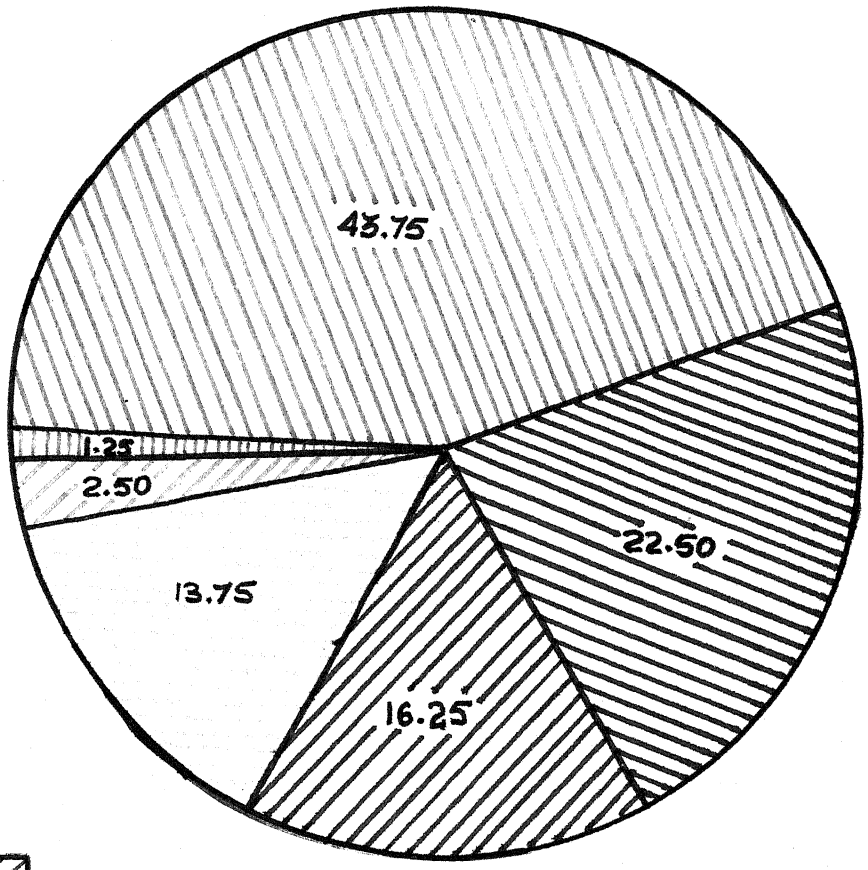
Comparison of pH of gastric juice before and after giving drug.

S.No.	Group	Mean pH* ± SEM Before giving the drug	Mean pH ± SEM An hour after giving the drug	Calculated t
1.	A	2.631 ± 0.1881	3.931 ± 0.3414	3.05
2.	B	2.275 ± 0.1242	5.1875± 0.2460	10.2373
3.	C	2.207 ± 0.1195	6.28 ± 0.1641	20.04
4.	D	2.4375± 0.1441	2.6563± 0.1699	0.9509
5.	E	2.431 ± 0.1622	6.088 ± 0.2572	11.6465

* The arithmetic mean of the pH values yields the same result that would be obtained by getting the geometric mean of the hydrogen ion concentrations, and converting it to a pH value (Feinstein, 1979).

The difference between mean pH ± SEM before and an hour after giving the drug is not significant statistically in group D, while it is highly significant in rest of the groups ($P < 0.01$) as shown above in table 7.

Fig. No. 2 - Showing type of Surgery done.



- General Surgery

- Obstetric and Gynaecological Surgery

- Orthopaedic Surgery

- E.N.T. Surgery

- Ophthalmic Surgery

- Dental Surgery

Table 8

Showing distribution of patients at risk before and after giving various drugs.

Group	Before giving drug				One hour after giving drug			
	Patients at risk (pH $\leq$ 2.5)		Patients not at risk (pH $>$ 2.5)		Patients at risk (pH $\leq$ 2.5)		Patients not at risk (pH $>$ 2.5)	
	No.	%	No.	%	No.	%	No.	%
A	9	56.25	7	43.75	2	12.50	14	87.50
B	12	75.00	4	25.00	1	6.25	15	93.75
C	12	75.00	4	25.00	-	-	16	100.00
D	8	50.00	8	50.00	5	31.25	11	68.75
E	10	62.50	6	37.50	-	-	16	100.00
Total	51	63.75	29	36.25	8	10.00	72	90.00

Above table clearly shows that out of eighty patients studied, fifty one (63.75%) were at risk i.e. the pH of gastric fluid was less than 2.5. It further shows that administration of Cimetidine significantly decreased the number of patients at risk.

DISCUSSION

D I S C U S S I O N

Aspiration of gastric contents into tracheo-bronchial tree, and the events that follow it, is a major problem after general anaesthesia, that every anaesthetist faces in his day to day practice. Silent regurgitation of gastric contents occurs more frequently than is realized, even with an endotracheal tube in place, no technique of anaesthetic induction provides a complete guarantee against aspiration and it might occur in the interval between induction and intubation or after extubation. The serious nature of this problem attracted the interests of many a scientist and it was Mendelson (1946) who stressed that the acidity of aspirate was the primary aetiologic factor in aspiration pneumonitis. Later Teabeaut (1952) established that pH below 2.5 produces pneumonitis like tissue reaction and the gastric secretion of higher pH produces approximately the same response as isotonic saline solution. Additional factors include the presence of particulate matter, and the volume of aspirate. Gastric fluid volume of 0.4 ml/kg body weight has been stated to

incur greater risk. However, Stoelting (1978) considers 20 ml (0.3 ml/kg body weight) as potentially hazardous.

As aspiration of gastric contents during operation is a major cause of anaesthesia related morbidity and mortality; this has, in recent years, led to renewed interests in pre-operative methods to reduce gastric acidity and volume, thus lessening the risk of serious pulmonary reaction following the aspiration of gastric contents.

Several drugs have been investigated in an attempt, to reduce acidity and volume of fluid prior to anaesthesia. Anti-cholinergic agents like Atropine and Glycopyrrolate have no significant effect in adult patients, but antacids do increase the pH of gastric contents, although the volume too increases or remains unaltered.

A recently developed Histamine H-2 receptor antagonist, Cimetidine, has been demonstrated to suppress the basal, meal stimulated, and nocturnal gastric secretion. It increases pH and decreases gastric volume and this has led to its use as an ideal pre-operative drug in the patients undergoing surgery, in order to minimize anaesthesia-related pulmonary aspiration problems.

Besides, many workers like Crawford (1956), Holmes (1956) and White (1959) have been emptying stomach pre-operatively using naso-gastric tubes, while others used large bore tubes to facilitate the removal of gastric contents during induction of anaesthesia (Macintosh, 1951; Wulfshon, 1957; Bizzarri et al, 1965).

With this in mind, the present study, spread over a period of one year, was undertaken to compare and evaluate the effect of various drugs i.e. antacid (Digene gel®) 30 ml orally, Atropine sulphate 0.65 mg i.m., Cimetidine 300 mg orally, and Cimetidine 300 mg i.v. (Tagamet®).

The patients were divided into five equal groups of sixteen each, depending upon the drug that was given to them (Table No. 1), an hour prior to induction of anaesthesia. All the five groups had nearly similar age, weight and sex distribution as also the ASA grading (Table Nos. 2, 3, 4 and 5). Assuming that not only emergency but routine surgical patients were also at risk of aspiration pneumonitis, the study comprised of elective surgeries from various surgical specialities (Table No. 6). All types of surgeries were chosen to obtain uniformity and conclusive results. In contrast, other workers have

mostly confined their works on emergency surgeries probably with the assumption that emergency surgical operations involve greater risk of developing aspiration pneumonia.

Much has been said and done to detect a critical pH and volume of the gastric fluid which renders a patient at risk and it is now almost universally accepted that a pH less than 2.5 and volume 20 ml or more is definitely hazardous (Vandam, 1965; Roberts and Shirley, 1974; Stoelting, 1978).

It is less commonly appreciated that patients fasting prior to elective surgery often arrive in the operating room with large gastric fluid volumes and a low pH. On the basis of pH alone, Coombs et al (1979) reported 82% of control patients with gastric fluid pH less than 2.5 at the time of intubation, Stoelting (1977) reported 63% patients (control group) with gastric fluid pH less than 2.5, while in our study fifty one (63.75%) patients had gastric fluid pH less than 2.5. Thus our results are in good agreement with those of Coombs et al (1979) and Stoelting (1977). Studies on anaesthetized patients by Gray et al (1953), Mahl et al (1953), Coombs et al (1979) and Kirkegaard et al (1980) demonstrated that 46 - 75% of the patients

will have a gastric fluid pH less than 2.5, thereby confirming our findings (Table No. 8). The increased number of patients presenting with a low pH can be explained on the basis of the fact that fear and apprehension as also fasting are known to increase gastric acid secretion, which undiluted because of fasting is highly acidic.

Shay and Sun have reported a prompt increase in acid secretion during insulin induced hypoglycemia, which suggests that acid secretion may increase during prolonged fasting. The fact that the stomach contents can be highly acidic during fasting has been amply demonstrated. Shay and Sun reported finding gastric contents of pH 2 to 1.3 during fasting, and Holmes (1956) found that some women in labour had gastric contents of pH 2.0 to 1.0.

EFFECT OF DRUGS :

Group A :- These patients were given antacid (Digene gel®) 30 ml orally an hour prior to induction of anaesthesia. Mean pH ± SEM before giving the drug in this group was 2.631 ± 0.1881 which increased to 3.931 ± 0.3414 an hour after the drug was administered, this, statistically speaking is highly significant ($P < 0.01$, Table No. 7). Nine patients (56.25%) had gastric fluid pH less than 2.5 before administering

the drug but only two patients (12.50%) had gastric fluid pH less than 2.5 an hour after the antacids were given (Table No. 8).

Taylor and Pryse-Davies (1966) measured the gastric fluid pH of ninty nine obstetric patients requiring emergency surgery. At the time of induction, of the fifty two control patients, 42.5% were found to have gastric fluid pH less than 2.5. The pH of gastric contents in the patients who were given Aluminium hydroxide or Magnesium trisilicate was 2.5 or less in 12.5% and 0% patients respectively. Thus our findings are in congruity with the above mentioned study. In Taylor and Pryse-Davies series (1966), 1.9 was the lowest pH in women who received Aluminium hydroxide while in the Magnesium trisilicate group, it was 4.6. In our study, the lowest pH was 2.0 and there had been a drop in the number of patients, from nine to two, with gastric fluid pH below the critical level.

Roper and Salem (1981) in their study have shown that overall frequency of patients, with gastric fluid pH less than 2.5, after having received Magnesium trisilicate was 35%, on the contrary it was 12.5% in our study. The possible explanation to this discrepancy may lie in fact that the amount of antacid (30 ml) used in the present study is more than that

used by the above workers (20 ml), moreover the drug used contained both Aluminium hydroxide and Magnesium hydroxide whereas others have used either Magnesium trisilicate or Aluminium hydroxide alone. Roberts and Shirley (1974) have shown conclusively that the use of antacids prior to caesarean section reduced the number of patients at risk from one in four to one in forty eight.

Lahiri et al (1973) reported that the single dose of 15 ml of 0.3 M Sodium citrate was effective in neutralizing gastric contents in emergency situation, where long term prophylactic measures have not been instituted. A dose of 10 ml of Magnesium trisilicate mixture administered 10-15 minutes prior to induction of anaesthesia was reported to maintain the pH above 2.5 during subsequent general anaesthesia for elective surgery and the effect sustained for 7 hr (Newson, 1977).

However the method of administration and sampling almost certainly introduced an error, since the antacids were instilled down the naso-gastric tube from which samples were withdrawn subsequently. Hester and Heath (1977) concluded that antacid was not uniformly effective in elevating gastric fluid pH, although it increased the volume of gastric fluid. Moreover, aspiration of antacid neutralized gastric

contents with a pH greater than 2.5 has been reported to produce significant pulmonary complications (Taylor, 1975). Gibbs et al (1979) reported antacid pulmonary aspiration in dog.

Group B :- Administration of oral Cimetidine (300 mg) an hour prior to induction of anaesthesia, increased the mean gastric pH ± SEM, in this group, from 2.275 ± 0.1242 to 5.1875 ± 0.2460, the average dose being 6.19 mg/kg body weight. The results observed were highly significant statistically ($P < 0.01$, Table No. 7). Twelve patients (75%) had gastric fluid pH less than 2.5 before giving the drug and this incidence decreased to one case (6.25%) after Cimetidine administration and the pH in this particular patient was 2.4.

Stoelting (1978) observed an 84% rise in gastric fluid pH above 2.5, 90 min. after administration of 300 mg Cimetidine orally, while on the contrary, it took only 60 min. for the drug to produce 93.75% results during the course of present study. The time gap difference can well be explained on the basis of the dose used i.e. 4.3 mg/kg body weight used by Stoelting as compared to 6.19 mg/kg in the present study, as has been shown that the duration and extent of H-2 receptor blockade increases with higher dose.

It can therefore be concluded that Cimetidine does produce a rise in gastric fluid pH, with the supportive evidence of the study of Husemeyer (1978), who administered 400 mg Cimetidine orally and found a 91.3% increase in the gastric fluid pH above the critical level of 2.5. The effects of drug have been found to bear no relationship of any kind with change in age, although Bond et al (1979), in contradiction to the present findings, mentioned greater rise in gastric fluid pH with advancing age, thereby, explaining that probably older patients are more sensitive to Cimetidine blockade, perhaps because of reduced population of H-2 receptors or functioning parietal cells with advancing age.

The time interval between administration of oral Cimetidine and induction of anaesthesia is not important, although some time for absorption (60-90 min) must be allowed.

Variability in individual patient's H-2 receptor sensitivities to Cimetidine may also exist. Gastric acid secretion by the parietal cells is stimulated by three endogenous agonists, Histamine, Gastrin, and Acetylcholine. Cimetidine antagonizes parietal cell acid secretion by all the agonists.

Tolerance of the drug by patients was excellent and no adverse effects were observed.

Group C :- Patients belonging to this group were injected Cimetidine (Inj. Tagamet®) 300 mg very slowly an hour prior to induction of anaesthesia, average dose being 6.08 mg/kg body weight. The mean pH ± SEM before and after the drug was 2.207 ± 0.1195 and 6.28 ± 0.1641 respectively, which is highly significant statistically ($P < 0.01$). Before the drug was administered, only four patients (25%) had gastric fluid pH above 2.5, but an hour after the drug administration gastric fluid pH values exceeded 2.5 in all the sixteen patients (100%) i.e. none of the patients had gastric fluid pH less than 2.5 after i.v. Cimetidine administration.

Coombs et al (1979) studied the effect of i.v. Cimetidine on gastric fluid pH. The mean dose administered was 4.5 mg/kg body weight. On the basis of pH alone, 82% of the control patients had gastric fluid pH less than 2.5 at intubation. In treated group there was progressive reduction in the number of patients with a pH below 2.5 with increasing time interval between Cimetidine administration and induction of anaesthesia ($P < 0.001$). None of the patients, receiving i.v. Cimetidine 60 min. prior to endotracheal intubation, had gastric fluid pH less than 2.5. It shows that results

observed are in congruity with those of Coombs et al. They also observed the effect of i.v. Cimetidine on gastric volume. Mean gastric volume decreased to less than one third of the control value when Cimetidine administration preceded induction of anaesthesia by an hour, with a 30 min. interval, the mean volume was less than 25 ml.

No untoward effects were observed in our patients receiving Cimetidine i.v. No change in vital signs occurred and there was no detectable alteration in the course of anaesthesia. Emergence from anaesthesia was also uneventful.

The duration of Cimetidine induced H-2 receptor blockade during general anaesthesia is not known, but the gastric pH remains above 2.5 for at least 3 hr.

Group D :- Anticholinergic drugs inhibit the basal gastric secretion. Inspite of their common use as pre-medicants, the effect of anticholinergics on gastric fluid pH and volume at the time of induction of anaesthesia have not been adequately studied in past.

Atropine sulphate 0.65 mg (average dose being 0.013 mg/kg body weight) injected an hour before the induction of anaesthesia did not produce encouraging

results in this group of patients. The mean pH ± SEM before and after the drug administration was 2.4375 ± 0.1441 and 2.6563 ± 0.1699 respectively, which is not significant statistically. Eight patients (50.0%) had gastric fluid pH below 2.5 before Atropine injection, their number came down to five (31.25%) an hour after the drug administration.

Salem et al (1976) studied the effect of Atropine (15-20 ug/kg body weight) i.m. an hour before induction of anaesthesia in children, and reported increased incidence of gastric fluid samples with pH values above 2.5. Before giving the drug, the incidence of patients with gastric pH above 2.5 was 7.4%, which increased to 17.6% following Atropine injection. It also resulted in a decreased volume.

Stoelting (1978) demonstrated that Atropine does not increase gastric fluid pH above 2.5 or reduce gastric fluid volume to less than 20 ml. Sixty three percent of patients (control group) had gastric fluid pH below 2.5, the incidence did not decrease significantly by the inclusion of Atropine and remained at 58%. A possible explanation of this differing values in our study from that of Stoelting can well be given by the fact that we had injected comparatively higher dose of Atropine (0.65 mg).

average weight of patients belonging to this group being 48.75 kg, in contrast to Stoelting's study who had administered smaller dose of drug i.e. 0.4 mg, average weight of patients being 73 ± 4 kg.

Group E :- Since anticholinergics and H-2 receptor antagonists presumably act through different mechanisms (antagonism of muscarinic action of Acetylcholine and blockade of H-2 receptors respectively), a combination of these two classes of drugs might be expected to lead to an additive effect, or even synergistic inhibition of gastric acid secretion. Although some workers have reported additive interactions between anticholinergics and Histamine H-2 receptor antagonists (usually employing a large dose of anticholinergic), others have been unable to show any further inhibitory effect by Atropine on H-2 receptor antagonists.

Patients were pre-medicated with Atropine 0.65 mg i.m. + Cimetidine 300 mg orally an hour prior to induction of anaesthesia. Average doses of Atropine and Cimetidine were 0.013 mg/kg body weight and 5.91 mg/kg body weight respectively. Mean pH ± SEM before the drugs were administered was 2.431 ± 0.1622 which significantly increased to 6.088 ± 0.2572 an hour after pre-medication. It is highly significant statistically ($P < 0.01$). Ten patients (62.50%) had

gastric pH below 2.5 before the combination of drugs was given, while it was well above 2.5 in all the sixteen patients (100%).

In the group B, where only Cimetidine 300 mg orally was given (6.19 mg/kg body weight), one out of sixteen patients we studied (6.25%) had gastric fluid pH below 2.5 (pH was 2.4) after the drug, whereas in this group none had gastric fluid pH below 2.5. It seems that combination of these two drugs had resulted in a synergistic effect.

A careful analysis of the data and above discussion supports the premise that Cimetidine would be an effective agent in the prophylaxis of aspiration pneumonitis and has several advantages over the usual antacids. Though pre-operative antacid administration results in significant increase in gastric pH, but several problems may, however, be associated with oral antacids. First, all emergency patients may not be candidates for oral antacids, second, aspiration of antacid neutralized gastric contents with a pH greater than 2.5 has been reported to produce significant pulmonary complications, third, an increase in gastric volume may also occur. Cimetidine i.v. obviates all these problems. Observations recorded clearly indicate that Cimetidine i.v. is the best agent for prophylaxis

of aspiration pneumonitis because it decreases volume too significantly, followed by combination of oral Cimetidine and anticholinergics. Anticholinergics alone are not significantly effective in increasing gastric pH. Oral Cimetidine alone increases gastric pH significantly. It is more palatable, increases gastric pH more consistently than antacids, and has a longer duration of action. Since there is no known hazard to single-dose administration of Cimetidine, it should be given "routinely" in a dose of 300 mg orally 60-90 min. prior to induction of anaesthesia in all cases undergoing surgery, especially if rapid induction and endotracheal intubation can not be anticipated.

SUMMARY AND CONCLUSIONS

SUMMARY AND CONCLUSIONS

Despite recent advances in anaesthesia and a great reduction in frequency of post-operative morbidity and mortality, aspiration pneumonitis still remains one of the most dreaded complications of anaesthesia and an important cause of anaesthesia related morbidity and mortality.

A competent anaesthetist using a safe technique, particularly during induction, with application of cricoid pressure and rapid tracheal intubation is obviously a pre-requisite, but despite this, reduction in gastric acidity is still a valuable safe-guard.

Several pharmacologic methods have been suggested to protect surgical and obstetrical patients from the severe pulmonary damage associated with gastric acid aspiration. All are directed at producing a gastric pH greater than 2.5 at induction of anaesthesia. Keeping this in mind, effect of antacids, Cimetidine and anticholinergics was studied on gastric pH, of

80 adult patients. Any patient exhibiting any disease or taking a drug, which alter gastric secretion or motility was excluded from this study.

After a careful review of the observations obtained and the discussion, the conclusions arrived at is summarised in the following lines -

1. A high proportion of surgical patients have gastric contents, the pH of which present a clinically significant risk of acid aspiration syndrome at the time of intubation.

2. Anticholinergics (Atropine sulphate) alone have no significant role in increasing gastric pH. Administration of 0.65 mg Atropine sulphate i.m. an hour prior to induction increased mean pH $\pm$ SEM from 2.4375 $\pm$ 0.1441 to 2.6563 $\pm$ 0.1699 which is not significant at all statistically.

3. Administration of oral antacids increases gastric fluid pH significantly. Mean pH $\pm$ SEM increased from 2.631 $\pm$ 0.1881 to 3.931 $\pm$ 0.3414, it is highly significant statistically ($P < 0.01$). There is significant decrease in number of patients at risk from nine to two. But it does not uniformly decreases gastric acidity and emergency patients are not amenable to this treatment. It is superior in comparison to anticholinergics alone.

4. Cimetidine 300 mg orally an hour prior to induction of anaesthesia has been found to be an effective agent in the prophylaxis of aspiration pneumonia. It has resulted in a significantly increased mean gastric pH ± SEM from 2.275 ± 0.1242 to 5.1875 ± 0.2460 ($P < 0.01$). Patients at risk were reduced from twelve to one following oral administration of Cimetidine 300 mg 60 min. prior to induction of anaesthesia. It increases gastric pH more consistently than antacid preparations. It is possible by pre-medication with oral Cimetidine to reduce the "high risk" group to a minimum.

5. Cimetidine i.v. is the best prophylactic agent available so far. None of the patients had gastric juice of pH less than 2.5 following Cimetidine 300 mg i.v. 60 min. prior to induction. There was marked pH change from 2.207 ± 0.1195 to 6.28 ± 0.1641 ($P < 0.01$). It has more rapid effect. It should be used as an effective adjunct to good anaesthetic technique and will reduce the risk of pulmonary damage if aspiration occurs in routine as well as emergency operations.

6. Combination of oral Cimetidine and anticholinergics is better than oral Cimetidine alone. Probably both drugs act synergistically.

Administration of i.v. Cimetidine is a costly affair and not easily available. So it is recommended that every patient should be given routine prophylaxis by oral administration of 300 mg Cimetidine or a combination of oral Cimetidine 300 mg and anticholinergics (Atropine sulphate 0.65 mg i.m.) an hour prior to induction of anaesthesia.

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